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| EXAMINER |
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DEVI, SARVAMANGALA J N

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| ART UNIT | PAPER NUMBER |
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1645

DATE MAILED: 09/24/2003

14

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/630,454

Applicant(s)

Liaw et al.

Examiner

S. Devi, Ph.D.

Art Unit

1645

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE three MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on Aug 11, 2003

2a) ☐ This action is **FINAL**.

2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) 1-23 ~~is/are~~ pending in the application.

4a) Of the above, claim(s) 1-5, 10 and 17-23 ~~is/are~~ withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) 6-8 and 11-16 ~~is/are~~ rejected.

7) ☒ Claim(s) 9 ~~is/are~~ objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.

2. ☐ Certified copies of the priority documents have been received in Application No. _____.

3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)

4) ☐ Interview Summary (PTO-413) Paper No(s). _____

2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)

5) ☐ Notice of Informal Patent Application (PTO-152)

3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____

6) ☐ Other:

Serial No. 09/630,454
Art Unit: 1645

RESPONSE TO APPLICANTS' AMENDMENT

Applicants' Amendment

- 1) Acknowledgment is made of Applicants' amendment filed 08/11/03 (paper no. 13) in response to the non-final Office Action mailed 06/04/03 (paper no. 12). With this, Applicants have amended the specification.

Status of Claims

- 2) Claims 6-8 have been amended via the amendment filed 08/11/03.
Claims 1-23 are pending.
Claims 6-9 and 11-16 are under examination.

Prior Citation of Title 35 Sections

- 3) The text of those sections of Title 35 U.S. Code not included in this action can be found in a prior Office Action.

Prior Citation of References

- 4) The references cited or used as prior art in support of one or more rejections in the instant Office Action and not included on an attached form PTO-892 or form PTO-1449 have been previously cited and made of record.

Rejection(s) Withdrawn

- 5) The rejection of claims 11-16 made in paragraph 7 of the Office Action mailed 11/05/02 (paper no. 9) under 35 U.S.C. § 112, first paragraph, as failing to provide an adequate written description of the invention and failing to provide an enabling disclosure, with regard to the deposit issue, is withdrawn in light of Applicants' amendments.
- 6) The rejection of claims 6-8 made in paragraph 20 of the Office Action mailed 06/04/03 (paper no. 12) under 35 U.S.C. § 101 as being directed to a non-statutory subject matter, is withdrawn in light of Applicants' amendments to the claims.
- 7) The rejection of claims 6-8 made in paragraph 21 of the Office Action mailed 06/04/03 (paper no. 12) under 35 U.S.C. § 112, first paragraph, as containing new subject matter, is withdrawn in light of Applicants' amendments to the claims.
- 8) The rejection of claim 9 made in paragraph 23 of the Office Action mailed 06/04/03 (paper no. 12) under 35 U.S.C. § 102(b) as being anticipated by Nakanishi *et al.* (US 4,657,860), is

withdrawn in light of Applicants' amendments to the base claim.

9) The rejection of claims 6-8 made in paragraph 24 of the Office Action mailed 06/04/03 (paper no. 12) under 35 U.S.C. § 102(b) as being anticipated by Sano *et al.* (US 4,436,170), is withdrawn in light of Applicants' amendments to the base claim.

Rejection(s) Maintained

10) The rejection of claims 6-8 made in paragraph 22 of the Office Action mailed 06/04/03 (paper no. 12) under 35 U.S.C. § 102(b) as being anticipated by Shijo *et al.* (US 5,077,207), is maintained for reasons set forth therein and herebelow.

Applicants contend that the '207 patent does not teach an ion chromatography operation nor a heat sterilization step. Applicants state that the '207 patent discloses a method for producing L-threonine, not L-lysine as the present application claims. Applicants submit that Shijo *et al.* do not teach or suggest the creation of a microorganism that grows on raffinate medium which has been heat sterilized and produces amino acids. Applicants assert that since the culture medium of the '207 patent is not the same as the claimed invention, nor does it disclose the creation of a raffinate-resistant organism, each and every limitation of the claims have not been met by Shijo *et al.* Applicants point to lines 3-8 on page 7 of the specification and state that 'raffinate' refers to a 'wastestream product from an ion exchange operation for lysine recovery'. Applicants point to the statement in the specification that '[s]terilization of a raffinate-containing medium using heat treatment produces amino acid derivatives and other metabolic antagonists which cause the inhibition of culture growth'.

Applicants' arguments have been carefully considered, but are non-persuasive. Contrary to Applicants' assertion, claims 6-8 are not limited to a bacterial strain that produces L-lysine. In other words, claims 6-8 do not exclude a bacterial strain producing L-threonine, but include an L-threonine-producing strain within their scope. With regard to the culture medium, Shijo's culture medium was sterilized by autoclaving, i.e., heat-sterilized (see Example 1); the prior art amino acid-producing bacterial strain did grow in this culture medium and therefore was resistant, as recited in the instant claims. This also suggests that sterilization of the prior art culture medium by autoclaving (heat sterilization) did not produce amino acid derivatives and other metabolic antagonists that inhibited culture growth. It should be noted that 'strain B' recited in part (c) of claim 6 is required

only to have the 'ability to grow in raffinate medium which has been heat-sterilized'. The 'bacterial culture medium' as recited in parts (b) and (c) of claim 6 is not required to be a 'heat-sterilized' raffinate-containing bacterial culture medium. The definition of the term 'raffinate' in the instant specification is not closed, and therefore, is not limited to a wastestream product from an ion exchange operation for lysine recovery. The specification at lines 4-6 on page 7 provides evidence that the description of 'raffinate' is not limited to a wastestream product from an ion exchange operation for lysine recovery, but is intended to broadly encompass ammonia sulfate, L-lysine, other amino acids, salts and carbohydrates. The prior art culture medium contains these substances. It is further noted that the feature upon which Applicants rely ('wastestream product from an ion exchange operation for lysine recovery') is not recited in the rejected base claim. Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993). Moreover, Applicants are reminded that the instant claims are product-by-process claims which are not limited to the manipulations of the recited steps, but only the structure implied by the steps. MPEP § 2113 states:

[E]ven though product-by-process claims are limited by and defined by the process, determination of patentability is based on the product itself. The patentability of a product does not depend on its method of production. If the product in the product-by-process claim is the same as or obvious from a product of the prior art, the claim is unpatentable even though the prior product was made by a different process. *In re Thorpe*, 777 F.2d 695, 698, 227 USPQ 964, 966 (Fed. Cir. 1985) (citations omitted).

A product does not have to be made by the same process in order to be the same product, because a product is a product, no matter how it is claimed. Applicants have not shown that the alleged difference(s) in the process results in a product that is structurally different from the product of the prior art. In the instant case, Applicants have not shown that the underlying structure of the prior art bacterial strain differs from that of the instantly claimed bacterial strain. The rejection stands.

Rejection(s) under 35 U.S.C § 112, Second Paragraph

11) Claims 6-8 and 11-16 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which Applicants regard as the invention.

(a) Claim 6 lacks proper antecedence for the recitation: 'strain B' (see line 8). Since this

limitation is not preceded by --said--, is this 'strain B' different from what is recited in line 1 of the claim, 'bacterial strain B', or 'raffinate-resistant bacterial strain' recited in the first line of part (c) of the claim?

(b) Claim 6 is vague, inconsistent and confusing in the recitation 'bacterial strain B' in line 1 of the claim and 'a raffinate-resistant bacterial strain B' in line 6 of the claim. The former limitation, 'bacterial strain B', is of much broader scope whereas the latter recitation, 'a raffinate-resistant bacterial strain B', is of much narrower scope.

(c) Claim 11 is vague, indefinite, incorrect and has improper antecedence in the recitation 'said mutant' (see line 8), because the earlier recitation in the same line is of 'mutants'.

(d) Claim 6 is vague, indefinite and is of confusing scope, because it is unclear whether or not the bacterial culture medium [recited in parts (b) and (c) of the claim] containing at least about 1% raffinate is indeed heat-sterilized.

(e) Claim 8 is incorrect in the recitation 'strain B produces and amino acid' (see line 2).

(f) Claim 11 has improper and/or confusing antecedence in the recitation 'the strain' (see last line). It is unclear where does the antecedence for 'the' comes from, because the strain recited in lines 1 and 2 of claim 11 is a 'L-lysine producing' strain, whereas the mutant from part (f) of the claim is one which produces any 'desired amino acid'. Are or aren't strains recited in parts (a) through (e) mutants themselves? It is further unclear how a strain specifically producing 'L-lysine' initially can show increased production of any 'desired amino acid' after mutagenesis. The recitation 'a desired amino acid as compared to the production of the same amino acid in the strain before being mutagenized' is further confusing, because it is unclear how would one make such a comparison. For example, a 'L-lysine producing' initial strain mutagenized to overproduce a heterologous 'desired amino acid', for example threonine, cannot be compared with the initial non-mutagenized strain which produces 'L-lysine'. The scope of claim 11 is internally inconsistent. Clarification/correction is requested.

(g) Claims 7 and 8, which depend from claim 6, and claims 12-16, which depend from claim 11, are also rejected as being indefinite because of the indefiniteness or vagueness identified above in the base claim.

Rejection(s) under 35 U.S.C § 112, First Paragraph

12) Claims 11-16 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The limitations in claim 11: 'L-lysine producing *Corynebacterium* strain said mutant strain has an increased amino acid production of a desired amino acid as compared to the production of the same amino acid in the strain before being mutagenized' do not have descriptive support in the specification, as originally filed. Applicants point to page 5 lines 12-13 and 22-28 and page 8, lines 11-12 as providing support for the limitations. However, these parts of the specification are not supportive of a mutant strain of the recited scope or function(s). Therefore, the above-identified limitations in the claim are considered to be new matter. *In re Rasmussen*, 650 F2d 1212 (CCPA, 1981). New matter includes not only the addition of wholly unsupported subject matter but also, adding specific percentages or compounds after a broader original disclosure, or even omission of a step from a method. See M.P.E.P 608.04 to 608.04(c).

Applicants are requested to remove the new matter from the claim(s), or point to specific page and line number(s) in the specification where support for such recitations can be found.

13) Claims 11-16 are rejected under 35 U.S.C. § 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a written description rejection.

It is noted that the 'mutants of (a), (b), (c), (d) or (e)' currently recited in the instant claim 11 do not exist independent of their function, i.e., increased amino acid production of 'a desired amino acid as compared to the production of the same amino acid in the strain before being mutagenized'. The specification discloses industrial applications or intentions for the claimed 'mutants'. However, the instant specification fails to teach a single 'mutant' of the 'L-lysine-producing' *Corynebacterium* strain NRRL B-300059, NRRL B-30060, NRRL B-30061, NRRL B30062 or NRRL B-30063, which mutant is capable of increased production of any 'desired amino acid', L-lysine or non-L-lysine, compared to the same amino acid in the strain before being mutagenized, as recited. Industrial applications minimally require an increased ability to produce any other broadly recited 'desired'

amino acid by the recited 'L-lysine producing *Corynebacterium* strain' after mutagenesis. However, such a *Corynebacterium* mutant strain having such an ability is neither disclosed, nor could be predictably or reproducibly constructed. A mere statement that the invention includes such a mutant is insufficient to meet the adequate written description requirement of the claimed invention. The *Written Description Guidelines* state:

There is an inverse correlation between the level of predictability in the art and the amount of disclosure necessary to satisfy the written description requirement. For example, if there is a well-established correlation between the structure and function in the art, one skilled in the art will be able to reasonably predict the complete structure of the claimed invention from its function.

The mutant has specific biologic properties dictated by the structure of the recited bacterial strain. A convincing structure-function relationship has to exist between the structure of the strain with the mutated gene and the function of the mutant strain. The function, i.e., increased production of any desired amino acid by an L-lysine producing *Corynebacterium*, cannot be predicted from the modification or mutagenesis of the strain. Applicants have not shown that mutagenesis of a reference strain initially producing L-lysine as claimed, would automatically predict the production of a mutant strain having the increased ability to produce any heterologous 'desired amino acid'. How would one make the comparison as recited, to determine that the mutant indeed has an increased production of any desired amino acid when the initial amino acid production by the parent strain is recited as being limited to L-lysine, is not described. The specification fails to teach the structure or relevant identifying characteristics of a representative number of mutant *Corynebacterium* species of NRRL B-30059, NRRL B-30060, NRRL B-30061, NRRL B30062 and NRRL B-30063, sufficient to allow one skilled in the art to determine that the inventors had possession of the invention as claimed. With the exception of NRRL B-30059, NRRL B-30060, NRRL B-30061, NRRL B30062 and NRRL B-30063, a skilled artisan cannot envision the detailed structure of all the species encompassed by the mutants recited in part (f) of claim 11. Regardless of the complexity or simplicity of the method of isolation, conception cannot be achieved until reduction to practice has occurred. Adequate written description requires more than a mere statement that its is a part of the invention and a reference to a potential method of isolating it. The mutants having the recited function(s)themselves are required. See *Fiers v. Revel*, 25 USPQ2d 1601, 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

Objection(s)

14) Claims 9 and 11 are objected to for the following reasons:

(a) In claim 9, for clarity, it is suggested that Applicants replace the recitation '10 g/l L-lysine' with --10 g/l of L-lysine--.

(b) To be consistent with the notation used in the specification at line 9 of page 12, it is suggested that Applicants replace the recitation 'NRRL B30062' with --NRRL B-30062-- in claim 11.

Remarks

15) Claims 6-8 and 11-16 stand rejected. Claim 9 is objected to. Claims 9 and 12-16 are free of prior art currently of record.

16) Papers related to this application may be submitted to Group 1600, AU 1645 by facsimile transmission. Papers should be transmitted via the PTO Fax Center located in Crystal Mall 1. The transmission of such papers by facsimile must conform with the notice published in the Official Gazette, 1096 OG 30, November 15, 1989. The CM1 facsimile center's telephone number is (703) 308-4242, which is able to receive transmissions 24 hours a day and 7 days a week. The RightFax number for submission of before-final amendments is (703) 872-9306. The RightFax number for submission of after-final amendments is (703) 872-9307.

17) Any inquiry concerning this communication or earlier communications from the Examiner should be directed to S. Devi, Ph.D., whose telephone number is (703) 308-9347. The Examiner can normally be reached on Monday to Friday from 7.45 a.m. to 4.15 p.m. except one day each bi-week, which would be disclosed on the Examiner's voice mail system. A message may be left on the Examiner's voice mail system.

If attempts to reach the Examiner by telephone are unsuccessful, the Examiner's supervisor, Lynette Smith, can be reached on (703) 308-3909.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

September, 2003


S. DEVI, PH.D.
PRIMARY EXAMINER